Rejections under judicially created doctrine of obviousness-type double patenting

Examiner has rejected several sets of Claims over co-owned U.S. Patents. A Terminal Disclaimer was filed on December 18, 2003, a copy of which is enclosed herewith. It is believed that the rejections are overcome.

Claims Rejections – 35 USC § 103

The Examiner has rejected Claims 1, 2 and 4-11 under 35 USC § 103 (a) as being unpatentable over Platz et al. (USPN 6,423,344 B1). The Examiner states that Platz teaches methods of delivering therapeutic agents such as insulin along with pharmaceutical carriers and excipients to the lung of a patient particles having a mass mean diameter of less than 10 microns and particles having a diameter of 0.4- 5 microns,

In fact, Platz teaches compositions for therapeutic administration, one route of which is by inhalation. The vast majority of the teachings require the particles to be less than 5 microns in size. Obviously, if the particles are less than 5 microns in size, then the mass mean diameter is less than 5 microns in size. At Column 2, line 9, it states that "The particles being delivered are usually less than 5 μm in size..." Platz states, at Column 2, lines 44-51:

> For pulmonary delivery, it is ***critical*** that the average particle size be maintained below 5 μm, preferably in the range from 0.4 μm to 5 μm, and that the amount of the composition comprising particles outside of the target size range be minimized. Preferably, at least 90% by weight of the powder will have a particle size in the range from 0.1 μm to 7 μm. More preferably, at least 95% will have a size in the range from 0.4 μm to 5 μm. (emphasis added.)

Platz states at Column 4, lines 12-16:

> It has been found that control of the concentration of the total solids below 5% significantly enhances the ability to obtain dried particles in the desired size range, i.e., below 5 μm, and preferably in the range from 0.4 μm to 5 μm.

Platz states at Column 5, lines 27-34:

> It has been found that proper control of the atomization and drying conditions can produce a dried powder having at least 90% of the mass of particles in the size range from 0.1 μm to 7 μm, more preferably having at least 95% in the size range from 0.4 μm to 5 μm, thus permitting the output of the drying step to be collected and the powder used without the need to size classify the product prior to packaging.

Platz states at Column 6, lines 14-17,

> Preferably, 90% by weight of the compositions will comprise particles having a particle size in the range from 0.1 μm to 7 μm, more preferably 95% in the range from 0.4 μm to 5 μm.

Platz states at Column 7, lines 63 et seq.:

> In particular, the dry particles will have an average particle size below 5 μm, more preferably being in the range from 0.4-5 μm, preferably from 0.4-4 μm, and most preferably from 0.4-3 μm. The average particle size of the powder will be measured as mass mean diameter (MMD) by conventional techniques.

Platz states at Column 8, lines 14-21:

> Usually, the ultrafine dry powders will have a size distribution where at least 90% of the powder by weight will comprise particles having an average size in the range from 0.1 μm to 7 μm, with preferably at least 95% being in the range from 0.4 μm to 5 μm. Additionally, it is desirable that the particle size distribution avoid having an excess amount of particles with very small average diameters, i.e., below 0.4 μm.

All of the compositions in Table 2 have particle sizes less than 5 microns.

Platz teaches that it is ***critical*** for pulmonary deliver for the particles to be less than 5 microns in size. While some of these citations permit particles to be present in the composition with a size of greater than 5 microns, the mass median diameter is not disclosed. Thus, where a powder has at least 90% of the powder in the 1-7 micron range, it doesn't necessarily follow that

the mass median will be greater than 5, thereby satisfying the claim limitation. Indeed, given the teaching of criticality, one would select a mass median diameter of less than 5 microns.

It is acknowledged that there are two sentences which is inconsistent with the above teachings. At Column 6, lines 4-9, it is stated that the "compositions comprises particles having an average particle size below 10 μm..." At Column 8, lines 25-27, it is taught that a particle size distribution having a mean between 3 and 10 microns will deliver to the central airways. However, this is clearly not a preferred embodiment.

Yet, this is not the only claim limitation that must be met by Platz to render the claimed invention obvious. The claims also require that the aerodynamic diameter be less than 4.7 microns. Nowhere does Platz teach the desired aerodynamic diameters of the particles. In Table 2, the mass median aerodynamic diameter for one run is disclosed as being 3.3 microns. This one run discloses an MMAD which is greater than the geometric diameter. That is, Platz makes very small particles (i.e., less than 5 microns) because he desires to deliver to the alveoli. Larger particles (i.e., greater than 5 microns) are taught to deliver to the central and upper airways.

The present inventors were the first to discover that improved compositions can be achieved by delivering large particles which behave like very small particles. Indeed, Applicants have been awarded a number of patents in this regard. For all the reasons the prior Examiners have granted the earlier patents, these claims are likewise not obvious over the teachings of Platz. Platz does not teach the combination of larger particles with lower aerodynamic diameters.

Furthermore, Platz teaches that the larger particles are delivered to the central and upper airways for treating asthma and chronic bronchitis. This is local delivery of the drug to the tissue that requires treatment. However, the claims are not directed to this kind of treatment. The claims are directed to the delivery of a hormone, such as insulin and testosterone, for systemic delivery. Furthermore, Platz in no way teaches that such particles will have the bioavailability to achieve a prolonged action of at least 4 hours.

Clearly, Platz does not teach that it is desirable and obvious to deliver a drug, such as a hormone (e.g., insulin or testosterone), for systemic delivery by administering a composition comprising large particles (e.g., having a mass mean diameter of greater than 5 microns) and a low aerodynamic diameter (less than 4.7 microns), as claimed.